

ASK A SPECIALIST**Ask a Pathologist: Again. Faster. The impact of MALDI-TOF technology on rapid microbial identification and changes in hospital practice**Jared S. Coberly¹, Harold M. Burgeson²¹Department of Pathology and Anatomical Sciences, University of Missouri, Columbia Missouri²Laboratory Services, University of Missouri Health Care, Columbia, Missouri

Corresponding author: Jared Coberly, MD. One Hospital Dr. Columbia, MO 65212 (coberlyj@health.missouri.edu)

Received: 3/12/19 Accepted: 3/14/19 Published: 3/25/19

Am J Hosp Med 2019 Jan;3(1):2019.003 <https://doi.org/10.24150/ajhm/2019.003>**Question**

I've heard about a new technology called MALDI-TOF for rapid identification of microbial organisms. What is it and how will it impact hospital medicine?

ANSWER

The benefit of rapid microbial identification is well known. Patients recover faster and have reduced lengths of stay when treated with optimal antimicrobial chemotherapy. De-escalation of antimicrobial chemotherapy is associated with improved survival.¹ Microbial organisms have long been characterized by their biochemical properties – a combination of their ability to grow on various media and their metabolic activity. Once an organism has been incubated and grown, sub-colonies are subjected to a battery of biochemical tests. While this process has been the gold standard of microbial identification for more than 100 years, incubation for growth and metabolic activity can take days. With the advent of gene sequencing techniques 25 years ago, more precise identification could be achieved by targeting ribosomal RNA and other housekeeping genes. However, sequencing techniques have not proven practical for routine identification as the technology comes at a significant cost: both financial and technical. Today, only very

large health systems or specialized laboratories offer ribosomal 16S RNA sequencing as part of their in-house test menu.

In the 1990s and early 2000s, investigators made tremendous advancement in the application of mass spectrometry towards rapid microbial identification. Technology known as “matrix-assisted laser desorption ionization time of flight” (MALDI-TOF) mass spectrometry can accurately identify individual species of bacteria, fungi, and mycobacterium at the first signs of growth. Ninety-eight percent of bacteria are identified at the genus level, with >90% resolving to a species-level identification. Less than 1% of organisms are identified incorrectly.² The technique is simple and rapid. Once a colony has formed, it is removed from the media, mixed with a UV-absorbing matrix, and placed on a steel target plate. A pulsed laser is directed at the preparation. The ionized particles are accelerated by electric potential through the mass spectrometer, which detects the particle's mass and charge. The spectral profile generated is compared against a

database of known and well characterized organisms from which the system generates a match (identification) and a reliability score. Current generation MALDI-TOF systems can complete identification on a 96-well target plate in one hour. On average MALDI-TOF reduces time to identification by 36 hours (Figure 1), with more significant improvements seen in certain specimen types. A 2017 study at the Michael J. Crescenz VA Medical Center demonstrated improvements in identification of organisms from abscess sources from 11 days to 6 days, bronchial washes from 6 days to 4 days, and anaerobic organisms (e.g., *Bacteroides fragilis*) from 6 days to 2 days.³ In 2013, the U.S. Food and Drug Administration (FDA) cleared the first commercial MALDI-TOF systems for clinical use.

But does MALDI-TOF's reduced time to identification improve time to optimal therapy? Multiple studies have demonstrated modest improvement in time to optimal therapy after the implementation of MALDI-TOF and subsequent shortened

duration of intravenous antimicrobial chemotherapy, reduced length of stay and decreased mortality. There is one important caveat: the reduced time to identification has little influence on the time to final susceptibility results, which still requires incubation of colonies with antimicrobial compounds and determination of the minimal inhibitory concentration (MIC). In some health systems using conventional biochemical methods and parallel testing of identification and susceptibility, final susceptibility results may only lag identification by a few hours. In these systems, some providers may be accustomed to waiting on the susceptibility results before de-escalating therapy. With the implementation of MALDI-TOF, susceptibilities may follow identification by 24 or 48 hours. The most impressive changes in time to optimal therapy have been seen in organizations with high clinical acceptance of, and response to, rapid identification results and those with strong antimicrobial stewardship programs.

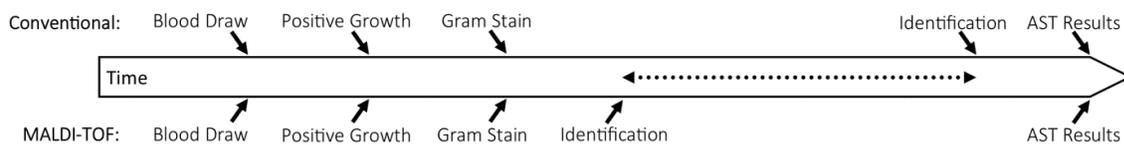


Figure 1. Compared to conventional laboratory methods, MALDI-TOF markedly reduces time to identification. MALDI-TOF: matrix assisted laser desorption ionization time of flight; AST: antibiotic susceptibility testing

Notes

Author contributions: All authors have seen and approved the manuscript, and contributed significantly to the work.

Financial support: Authors declare that no financial assistance was taken from any source.

Potential conflicts of interest: Authors declare no conflicts of interest.

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